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Review

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Superior vena cava syndrome

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ABSTRACT

Superior vena cava syndrome is the general name for the symptoms and presentation due to acute obstruction or occlusion of the superior vena cava flow. It usually develops secondary to underlying malignancies and is a life-threatening oncologic emergency. In this review, the current clinical approach to superior vena cava syndrome, including the etiologic considerations, investigations that should be planned, diagnosis, and treatment algorithms, is reviewed.

Keywords: Superior vena cava syndrome, oncology

INTRODUCTION

Superior vena cava syndrome (SVCS) is the name given to the symptoms and general picture that develop due to obstruction or occlusion of blood flow in the superior vena cava, which consists of a thin wall, and it is a condition that may have a mortal course.[1,2] It frequently occurs due to thrombus formation or infiltration of the vessel wall by malignant cells.

ANATOMY AND PHYSIOLOGY

The superior vena cava (SVC) is a very important structure that provides venous drainage of the head, neck, upper extremities, and upper thoracic region and accounts for one-third of the total venous return to the heart. It is structurally thin-walled and valveless, which makes it highly sensitive to compression by surrounding lesions. The SVC is formed by the junction of the right and left brachiocephalic veins at the inferior posterior aspect of the right first costa. The venous structures constituting the SVC are summarized in Figure 1.[3]

Figure 1. Venous structures forming the SVC

The SVC travels along the mid-upper part of the mediastinum and empties into the right atrium of the heart at the level of the third intercostal space. This journey of the SVC is approximately 7 cm, and the vessel width is around 2 cm. The SVC is frequently exposed to obstruction or compression due to the many structures in its neighborhood. These structures include the sternum and trachea, the pulmonary artery, the right bronchus, and surrounding lymph nodes. In addition, infiltration due to malignancies may also lead to obstruction. When obstruction develops in the SVC, alternative routes to the right atrium are formed through collateral vessels due to increased pressure in the surrounding veins. It takes several weeks for collaterals to become evident after obstruction. The most important structures providing these pathways are the azygos vein, hemiazygos vein, internal mammary vein, and lateral thoracic vein. Venous pressure decreases with the effect of collateral vessels. However, this decrease in pressure is transient, and if the underlying cause is not eliminated, the pressure rises again, and the classical symptoms of SVCS are established. Especially in obstructions below the azygos vein, the clinic develops more rapidly and more prominently.[4,5]

Recognizing anatomic variations is becoming increasingly important with the increasing frequency of interventional treatments in recent years. The most common congenital anomaly of the SVC is persistent left SVC, and its frequency in the general population is approximately 0.4%.[6]

ETIOLOGY

While infectious causes (such as tuberculosis and syphilis) were frequently observed in the etiology of SVCS in the past

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few years, malignancies are now at the forefront. Malignant causes constitute approximately 70% of the etiology. Among malignant causes, non-small cell lung cancer (NSCLC) ranks first. It has been found that approximately 50% of all malignant causes originate from NSCLC. The second most common cause is small cell lung cancer (SCLC), with a prevalence of approximately 25%. These are followed by lymphoma subtypes. The etiology of SVCS is summarized in Table 1.[2]

Table 1. Etiologic causes in superior vena cava syndrome

Malignant causes (about 70%)	Benign causes (about 30%)
NSCLC SCLC Lymphomas (especially NHL) Thymoma Other mediastinal and metastatic cancers	Mediastinal fibrosis Thrombosis Tuberculosis and fungal infection Vasculitis (often Behcet's syndrome) Radiation-induced fibrosis Aortic aneurysm Sarcoidosis and silicosis

Among benign causes, the increased use of intravenously implanted devices such as pacemakers, port catheters, and implanted defibrillators, especially in the last decade, paves the way for SVCS by bringing thrombotic side effects and increasing its incidence. In clinical studies, it has been observed that 28% of all SVCSs are device-related.[2] The frequency of benign causes of SVCS not related to devices and catheters is decreasing day by day. Patients with SVCS due to benign causes are generally younger and have a longer life expectancy.[7-10]

EPIDEMIOLOGY

The incidence of SVCS is reported to be approximately 15,000 cases per year in the USA, and studies show that the incidence is increasing. In the literature, the incidence of SVCS is between 1/650 and 1/3100. In clinical studies, it has been determined that the incidence has increased, especially in recent years, as a result of the increase in the use of catheters, pacemakers, and defibrillators.[11]

CLINICAL FINDINGS AND DIAGNOSTIC APPROACH

Clinical findings in SVCS present a wide range and vary according to the severity of obstruction, anatomical localization, rate of development, etiologic cause, and performance of the patient. The most common clinical findings include facial and neck edema, neck and chest vein engorgement, watery eyes, and upper extremity edema. These clinical findings and their frequencies are compiled in Table 2.[12]

In patients with SVCS developing due to malignant conditions, a sudden increase in venous pressure may occur due to the rapid occlusion of the SVC. Life-threatening cerebral and laryngeal edema may develop in these patients.[12] Clinical findings are sufficient for the diagnosis of SVCS in many patients. Confirmation of the diagnosis with radiologic imaging is not essential.Although it is important to make a diagnosis in a patient with SVCS clinic, it is also essential to determine the etiology of this condition and the subtype of malignancy, if any.

Table 2. Symptoms and clinical findings in superior vena cava syndrome

Symptoms and Findings		Frequency of Occurrence
Hemodynamic findings	Facial edema	82%
	Edema in the arms	46%
	Fullness in the neck veins	63%
	Fullness in the chest veins	53%
	Facial plethora	**20%**
Respiratory finding*	Symptoms related to vision	2%
	Dyspnea	54%
	Cough	54%
	Hoarseness	17%
	Stridor	4%
	Syncope	10%
Neurological findings	Headache	9%
	Dizziness	6%
	Confusion and stroke	6%

A detailed history and a good physical examination are very important for patients with clinically suspected SVCS. The severity of the clinic is of great importance in terms of the need for urgent treatment. A scoring system evaluating the severity of the clinic in SVCS syndrome has been organized and is presented in Table 3.[13]

Table 3. Clinical severity classification of patients with superior vena cava syndrome

	Severity		Description
0		10%	Radiologic findings, no clinical findings
1	Lightweight	25%	Head and neck edema, cyanosis, plethora present
2	Middle	50%	Accompanied by functional impairment (difficulty swallowing, cough, restriction of neck and eye movements, visual impairment, etc.)
3	Heavy	10%	Mild/moderate brain edema (headache, dizziness, mild laryngeal edema, syncope)
4	Life-threatening	5%	Severe cerebral edema (confusion), severe laryngeal edema (stridor), severe hemodynamic problems (syncope without triggering factor, hypotension, renal failure)
5	Fatal	<1%	Death

Radiologic studies are important to determine the etiologic cause, to determine the secondary interventional diagnostic method, if any, and to determine treatment management rather than diagnosis. For example, a mediastinal mass can be diagnosed with a simple chest radiograph, but the method that will present the content of the tissue and its relationship with surrounding tissues in detail will be computed tomography.

Contrast-enhanced computed tomography (CT) is particularly preferred in these patients. Contrast-enhanced CT is the best method of visualization of the SVC and is also very helpful in determining the site of endovascular intervention for patients for whom intervention is planned.14 Computed tomography, especially in the venous phase, is important in terms of a

better evaluation of the VCS. Contrast venography is of great importance in patients in whom stent placement or operation is planned. This method provides the most detailed and accurate information about the location and degree of obstruction and accompanying thrombosis in the SVCS.[15]

The radiologic classification of SVCS was made by Stanford et al.[16] and is presented in Table 4.

Table 4. Radiological classification of superior vena cava syndrome

Type 1	There is a mild degree of stenosis <90%
Type 2	There is severe stenosis >90%
Type 3	There is complete obstruction but the mammary and epigastric veins do not participate in collateral flow.
Type 4	There is complete obstruction, the mammary and epigastric veins participate in the collateral flow.

Since the treatment of SVCS is targeted at the underlying disease, histopathologic diagnosis before treatment is very important. Currently, the most commonly used method is transbronchial fine needle aspiration biopsy with bronchoscopy, and the diagnosis rate is quite high. Nevertheless, all diagnostic methods should be evaluated, and the most appropriate choice should be made for the patient. In a retrospective study, the methods used in histopathologic diagnosis and their diagnostic rates are shown in Table 5.[17]

Table 5. Histopathologic diagnostic methods and rates of use in superior vena cava syndrome diagnosis

Diagnostic Method	Rates of Use in Diagnosis
Fiberoptic Bronchoscopy	65.7%
Transthoracic biopsy	17.1%
Video thoracoscopy	8.6%
Mediastinoscopy	5.7%
Peripheral lymph node excision	2.9%

TREATMENT APPROACH

Patients diagnosed with SVCS should definitely be followed up in a multidisciplinary manner. In order to evaluate different treatment options, especially oncology, pulmonology, radiology, radiation oncology, and surgery, specialists should follow the patient closely.[18]

There are two main components of treatment for patients diagnosed with SVCS. These can be listed as symptomatic palliation and treatment of the underlying disease. Conservative treatment is applied until the underlying disease is diagnosed. Although there are many opposing views on conservative treatment, the definitive methods are bed rest, bed head elevation, oxygen support, and balanced fluid intake. The first conservative treatment is the elevation of the head of the bed. The aim of elevating the head of the bed is to decrease the hydrostatic pressure in the head and neck and to decrease the clinical findings of SVCS.[19]

There are also methods that are recommended but for which there is no definite data on their usefulness. These can be listed as diuretics and corticosteroids. Diuretics show their effect by decreasing intravascular pressure in venous structures distal to the obstruction. Corticosteroids are especially effective in corticosteroid-sensitive malignancies, but their use is recommended for a limited period.[12]

Clinical severity staging is very important in specific treatment for underlying conditions. In such patients, there are different approaches depending on the stage. This approach is summarized in Figure 2.[17]

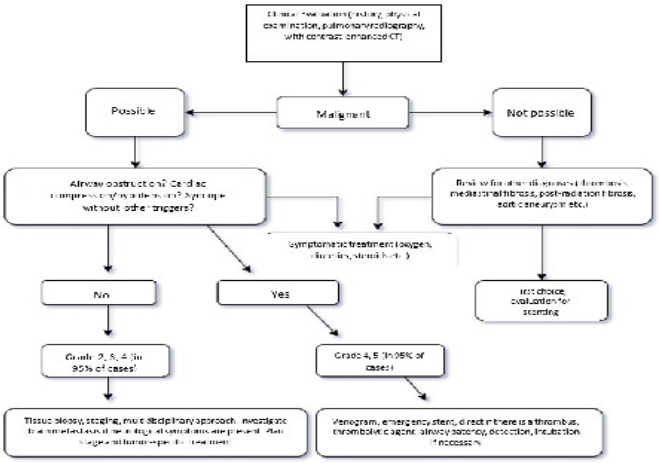

Figure 2. Clinical approach algorithm for a patient with superior vena cava syndrome

Until the recent past, radiotherapy was considered an emergency and first-line treatment for SVCS. However, new studies have looked into other options because radiotherapy has a lower chance of making a histopathologic diagnosis, symptoms can last up to three weeks longer, and the effects are only temporary. With the development of vascular intervention technologies, endovascular stent applications have been shown to improve symptoms faster and more effectively.[20-22]

Among endovascular therapies, especially stenting, has become the standard approach for SVC obstruction for both benign and malignant etiologies in the last 2 years. The benefits of this treatment include a high success rate and a low complication risk. In addition, it does not affect the histopathologic diagnosis and can be used in combination with chemoradiotherapy.[19]

Balloon angioplasty alone is an approach that does not require additional treatment, rapidly restores flow, and provides symptom improvement. However, early restenosis and reocclusion are frequent due to external compression and the fibroelastic structure of the perivascular tissue. Therefore, current guidelines recommend stent placement in most cases of SVC occlusion. Correct stent selection is important in these patients. Stent selection depends on many factors, including the severity of SVC obstruction, length, tortuosity, and resistance to dilatation.[23,24] Accordingly, the most commonly used stents are balloon-expandable stents, self-expanding wall stents, and Gianturco Z-stents.[25]

Unfortunately, surgical options are limited in SVCS. It is considered in cases of severe occlusion and thrombosis of

the collaterals. It is usually a quick and permanent solution. However, its invasiveness causes it to lag behind other options. Chemotherapy/radiotherapy may be preferred due to their high sensitivity, especially in cases caused by SCLC. The commonly used regimen is the platinum-etoposide combination. In NSCLC, radiotherapy is more prominent. There are clinical studies showing that the use of targeted agents is also beneficial. Another important method is endovascular stenting. It can be used alone or in combination with chemoradiotherapy. Clinically, it has been shown to be roughly 90% effective. It should be considered as the first choice, especially in cases requiring urgent intervention.[9,26]

The prognosis of SVCS depends on the underlying cause and treatment. The prognosis is generally poor in patients with cancer. In SVCS caused by thrombosis or mediastinal mass, it is possible to improve symptoms and prognosis with treatment.

CONCLUSION

SVCS is a constellation of clinical signs and symptoms that result from partial or complete obstruction of the SVC. In addition to early diagnosis, significant advances are also needed in the treatment of SVCS. Targeted therapies and immunotherapies can offer patients more effective treatment options with fewer side effects.

SVCS also has psychological and social dimensions, in addition to physical ones. Therefore, psychosocial support and rehabilitation programs should also be developed to help manage symptoms and improve patients' quality of life.

We believe that future research will play a key role in the fight against superior vena cava syndrome (SVCS). The primary objective of this research is to review the current approach to superior vena cava syndrome and to pave the way for future treatment modalities.

ETHICAL DECLARATIONS

Referee Evaluation Process
Externally peer-reviewed.

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The authors have no conflicts of interest to declare.

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All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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